This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No. 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. REGISTRATION NO. 50-R-0004 **CUSTOMER NO.** 42

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include Zip Code)*

ASTRA ZENECA PHARMACEUTICALS
VET MED DEPT PO BOX 15437 1800 CONCORD PK
WILMINGTON, DE 19850-5437

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS*(sites)*

(b)(2)High, (b)(7)(F)

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use APHIS FORM 7023A)*

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic,analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs		30	30	1	61
5. Cats					
6. Guinea Pigs	42	196	368	210	774
7. Hamsters					
8. Rabbits					
9. Non-Human Primates					
10. Sheep					
11. Pigs					
12. Other Farm Animals					
13. Other Animals					
Gerbils			5		5
Ferrets				24	24

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all the exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional official)
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)*	DATE SIGNED
(b)(6), (6)(7)(C)		11/12/2008

APHIS FORM 7023 **(AUG 91)** (Replaces VS FORM 18-23 (Oct 88), which is obsolete

PART 1 - HEADQUARTERS

NP

APHIS Form 7023 Column E Explanation

This form is intended as an aid to completing the APHIS Form 7023 Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

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1. Registration Number: 50-R-0004

2/3. Species (common name) & Number of animals used in this study:

Ferrets (24)

4. Explain the procedure producing pain and/or distress.

Assessment of Emetic and/or Anti-emetic potential in Ferrets: Safety Pharmacology studies are performed to determine whether potential candidate drugs and lead compounds have either emetic or anti-emetic properties. Anti-emetics have transformed the management of patients undergoing chemotherapy and radiation therapy for cancer. New drug candidate may prove more effective in man against delayed emesis induced either by cisplatin, post-operative nausea and vomiting, or motion sickness. Additional studies will be performed to complete its general pharmacology profile by determining whether the drug of interest has emetic potential. This latter experimental paradigm is performed most frequently. Compounds will be pre-selected for testing based upon pharmacological profile from various drug discovery efforts. There are no in vitro models of emesis, but there are several established animal models of emesis in dogs, cats, ferrets, rats, and gerbils. Ferrets respond to the same emetics and anti-emetics as humans and a large body of literature characterizing the species emetic responses and associated behaviors exists. Because of the homology with humans and extensive characterization both within and outside of the company, fewer animals are needed to obtain statistically significant results and the ferret is the species of choice.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

Animals in this category are given an emetic agent or compound which causes vomiting and retching. The objective of these studies is to determine experimental compounds effects on the emetic response. In order to evaluate this effect, we cannot alleviate these distress responses with drugs that would confound the results and invalidate the data.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: CFR:

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1. Registration Number: 50-R-0004

2/3. Species (common name) & Number of animals used in this study:

Guinea Pigs (210)

4. Explain the procedure producing pain and/or distress.

Separation-induced vocalizations in guinea pig pups: Pups are placed individually in a testing box that is isolated from the home cage for a period not exceeding 15 minutes and the duration of vocalization is recorded. Experimental compounds effects on this response is evaluated after a control session.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

These studies are designed to assess compounds in an animal model of human affective disorders; therefore alleviation of distress would make this behavioral assay invalid.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: CFR:

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1. Registration Number: 50-R-0004

2/3. Species (common name) & Number of animals used in this study:

Dogs (1)

4. Explain the procedure producing pain and/or distress.

Pharmacokinetic and /or Absorption, Distribution, Metabolism and Excretion in Dog : Compounds studied using this procedure have previously gone through a pharmacological screening cascade (in vitro and in vivo) and have demonstrated acceptable pharmacological activity. Metabolism and disposition studies are necessary to support the pharmacological and toxicological evaluation of compounds. The metabolism and disposition of a compound is the result of multiple processes (absorption, distribution, metabolism and excretion) that cannot be adequately simulated by in vitro or computer models. Dogs are administered experimental compounds and blood samples are taken at selected time points to determine the metabolic profile. Urine and feces may also be collected and analyzed.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

In rare instances an experimental drug candidate may have unanticipated adverse effects. The single dog in this category had an unexpected adverse event and was evaluated by a staff veterinarian. The veterinarian determined the clinical evaluation of neurotoxicity characterized by intermittent behavioral changes, shifting motor deficits and systemic impact. The animal was humanely euthanized as a result of this diagnosis and a necropsy was performed. Administration of drugs to alleviate the adverse reaction could have confounded histopathological analysis and invalidated the experiment.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: CFR: